

## **How to Use ENBREL<sup>®</sup> (etanercept)**

### **INSTRUCTIONS FOR PREPARING AND GIVING AN INJECTION**

#### **Introduction**

The following instructions are for preparing and giving a dose of ENBREL. ENBREL is given as an injection under the skin. ENBREL should be used under the guidance and supervision of a doctor. Your/your child's doctor or nurse will assist you in preparing and injecting your first dose (or first few doses) of ENBREL. Do not attempt to prepare or inject ENBREL on your own until you understand how to mix and inject a dose. If you are having difficulty giving an injection, we encourage you to ask a family member or other caregiver who is able to help you with your injections to become involved with your treatment and learn how to give your injection.

**DOSING FOR PEDIATRIC PATIENTS:** The appropriate dose for your child will vary depending on your child's body weight. Your child's doctor will inform you of the correct amount of drug to use.

**SINCE THE PRODUCT WAS FIRST INTRODUCED, SERIOUS INFECTIONS, SOME INVOLVING DEATH, HAVE BEEN REPORTED IN PATIENTS USING ENBREL. MANY OF THESE INFECTIONS OCCURRED IN PATIENTS WHO WERE PRONE TO INFECTIONS, SUCH AS THOSE WITH ADVANCED OR POORLY CONTROLLED DIABETES. RARE CASES OF TUBERCULOSIS HAVE ALSO BEEN REPORTED. ENBREL SHOULD BE DISCONTINUED IN PATIENTS WITH SERIOUS INFECTIONS. DO NOT START ENBREL IF YOU HAVE AN INFECTION OF ANY TYPE OR IF YOU HAVE AN ALLERGY TO ENBREL OR ITS COMPONENTS. ENBREL SHOULD BE USED WITH CAUTION IN PATIENTS PRONE TO INFECTION. CONTACT YOUR/YOUR CHILD'S**

**PHYSICIAN IF YOU HAVE ANY QUESTIONS ABOUT ENBREL OR INFECTIONS.**

There have been rare reports of serious nervous system disorders such as multiple sclerosis, seizures or inflammation of the nerves of the eyes. Tell your doctor if you have ever had any of these disorders or if you develop them after starting ENBREL. There have also been rare reports of serious blood disorders, some involving death. **Contact your doctor immediately if you develop symptoms such as persistent fever, bruising, bleeding, or paleness.** It is unclear if ENBREL has caused these nervous system or blood disorders. If your doctor confirms serious blood problems, you may need to stop using ENBREL.

In medical studies some people reported redness, itching, pain, swelling, bleeding, and/or bruising where the injection was given (Injection Site Reactions or ISRs). If you experience any of these symptoms and they concern you, contact your/your child's doctor, nurse, or pharmacist.

The most frequent adverse events in placebo-controlled clinical trials involving 349 adults were ISR (37%), infections (35%), and headache (17%). Only the rate of ISR was higher than that of placebo. The most frequent adverse events in a methotrexate-controlled clinical trial of 415 adults with early-stage RA were infections (64%), ISR (34%), and headache (24%). Only the rate of ISR was higher than that of methotrexate. In all 1,197 RA patients studied, malignancies were rare (1%).

*NOTE: The needle cover is made from latex. If allergic to latex, talk to a doctor before using.*

ENBREL dose trays should be stored in the refrigerator at 36° to 46°F (2° to 8°C) both before and after the powder is mixed with the diluent. Solution of ENBREL

(powder mixed with diluent) must be discarded if not used within 6 hours. *DO NOT* freeze ENBREL.

Any questions about therapy with ENBREL (for example, what to do if you miss a dose) should be directed to your/your child's doctor, nurse, or pharmacist. A toll-free information service is also available: 1-888-4ENBREL (1-888-436-2735).

There are three methods of preparing the ENBREL dose for injection.

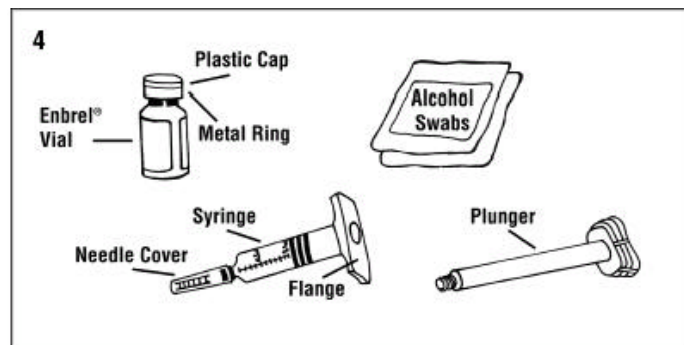
The first method is the *Dosing System* starter kit, which is not a part of this package, that contains tools designed to help you prepare and administer the product. Each *Dosing System* contains a "mixing station" device that helps keep the needle in line with the center of the vial stopper and guide the needle into the vial correctly. The *Dosing System* starter kit is available at no charge upon request through your/your child's doctor, or by delivery to your/your child's doctor by calling 1-888-4ENBREL. If you choose to use the "mixing station" method, follow the instructions provided in the video tape and "Step-by-Step Visual Guide" book instead of Step 3 below. The video tape and "Step-by-Step Visual Guide" book are provided with the separately available *Dosing System* starter kit.

The following instructions are for the other two methods of preparing and giving a dose of Enbrel; the free-hand method (Step 3A) or the dose preparation guide method (Step 3B). The dose preparation guide is on the underside of each dose tray provided with the product.

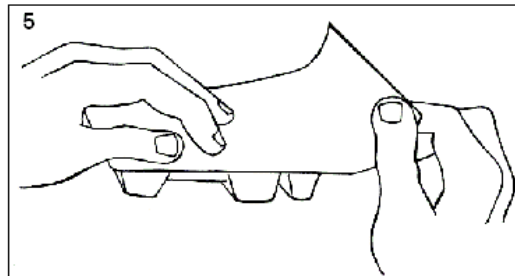
### **Step 1: Setting up for an injection**

1. Select a clean, well-lit, flat working surface.
2. Take the ENBREL dose tray out of the refrigerator and place it on a flat surface.

3. Wash your hands thoroughly with soap and warm water.
4. The dose tray should contain the items shown below. (If not, don't use the dose tray and consult your pharmacist.) Use only these items. The prefilled diluent syringe is specially designed for the preparation and administration of ENBREL. Do not use any other syringe.



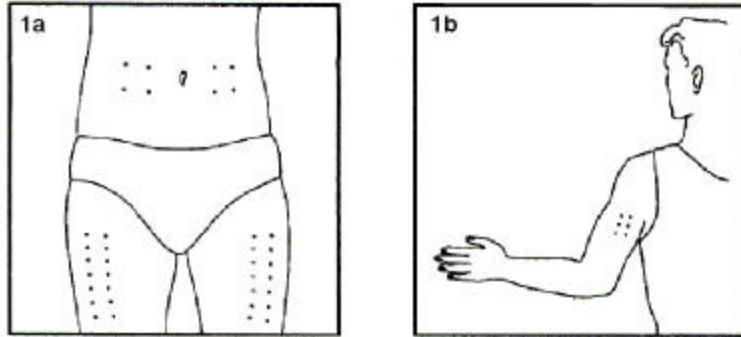
5. Peel the paper seal off the tray.



6. Inspect the expiration (Exp.) dates on both the vial label and syringe label. They should be the current month and year or later. (If not, don't use them and consult your pharmacist.)

## Step 2: Choosing and preparing an injection site

1. Choose an injection site on the thigh, stomach, or the back part of the upper arm.



2. Rotate sites with each new injection. Make sure that the new injection is given at least one inch from an old site. Do not inject into areas where the skin is tender, bruised, red, or hard. (It may be helpful to keep notes on the location of the previous injections.)
3. To prepare the area of skin where ENBREL is to be injected, wipe the injection site well with an alcohol swab, using a circular motion. **DO NOT** touch this area again before giving the injection.

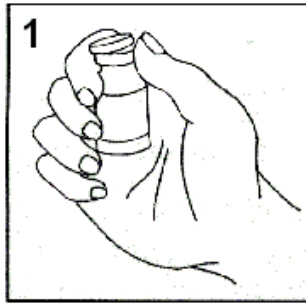
## Step 3: Prepare the ENBREL dose for injection

Consult your/your child's doctor about the appropriate method to use to prepare an ENBREL dose for injection. Two methods are described below.

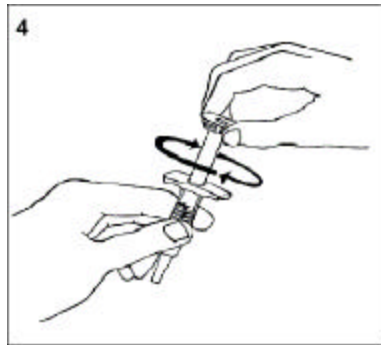
**To use the free-hand method start with Step 3A. To use the Dose Preparation Guide method (on the underside of the dose tray) start with Step 3B.**

### **Step 3A: Free-hand**

1. Remove the plastic cap from the ENBREL vial. Do not remove the gray stopper or metal ring around the top of the vial.

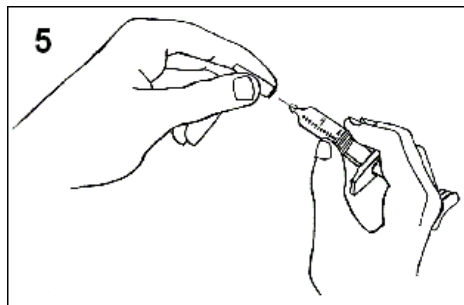


2. Use a new alcohol swab to clean the gray stopper on the ENBREL vial. After cleaning, place the ENBREL vial upright on a flat surface. Do not touch the stopper with your hands.
3. Slide the plunger into the syringe.
4. Turn the plunger clockwise until a slight resistance is felt. (That is, until more force is



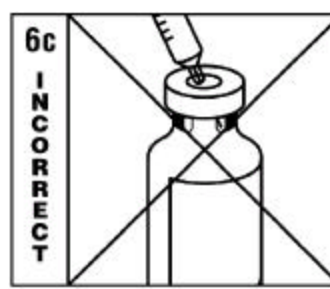
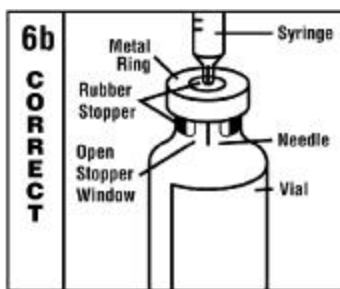
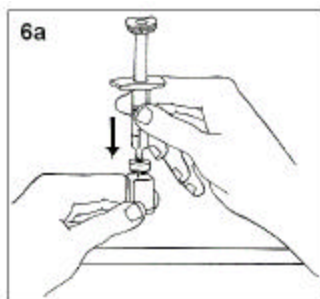
required to turn the plunger.)

5. Pull the needle cover straight off the syringe. **DO NOT** touch the needle or allow it to touch any surface.

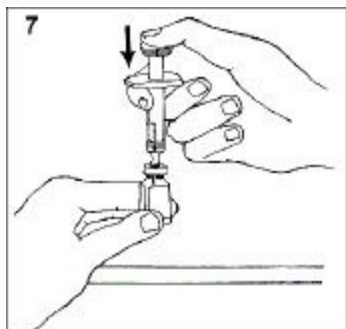


### ***ADDING DILUENT***

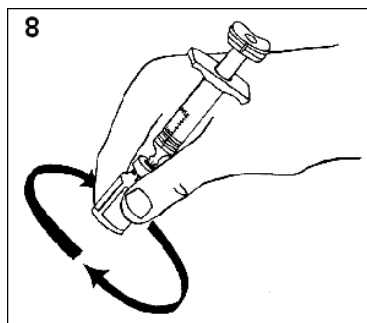
6. With the ENBREL vial upright on a flat surface, such as a table, insert the needle straight down through the center ring of the gray stopper. If the needle is correctly lined up, you should feel a slight resistance and then a “pop” as the needle goes through the center of the stopper. Look for the needle tip inside the stopper window (see Illustration 6.b). If the needle is not correctly lined up with the center of the stopper, you will feel constant resistance as it goes through the stopper and no “pop”. The needle may then enter at an angle and bend, break or prevent proper addition of diluent into the vial (see Illustration 6c).



7. Push the plunger down **VERY SLOWLY** until all liquid from the syringe is in the vial. Adding the liquid too fast will cause a lot of foaming (bubbles).



8. Leave the syringe in place. Gently move or swirl the vial in circles a few times, to dissolve the powder. **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colorless. After the powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do not inject the solution if it contains lumps, flakes, or particles.** If all the powder in the vial is not dissolved or there are particles present, call 1-888-4ENBREL (1-888-436-2735) for assistance.

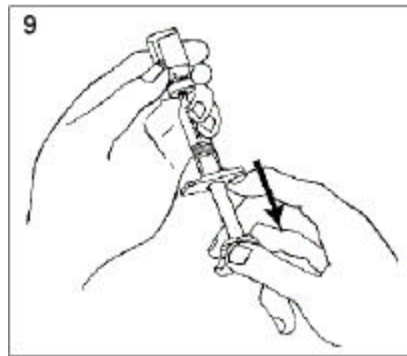


#### ***WITHDRAWING THE ENBREL SOLUTION FROM THE VIAL***

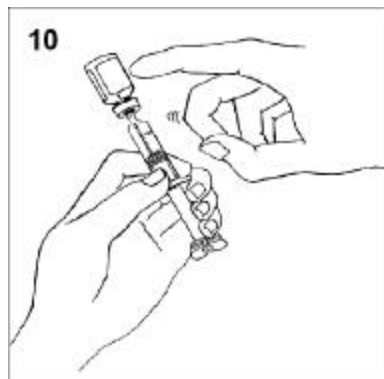
9. With the needle still in the vial, turn the vial upside down at eye level. Slowly pull the plunger back to draw the solution into the syringe. Use the “mL” markings on the side of the syringe to withdraw the appropriate dose as directed by your/your



child's doctor. For adult patients, remove the entire volume (1 mL of solution), unless otherwise directed by your doctor. For pediatric patients, remove only the portion of the 1 mL solution as directed by your child's doctor. As the solution level drops in the vial, you may need to partially withdraw the needle to keep the tip of the needle in the solution. Some white foam may remain in the vial — this is normal.



10. With the needle still inserted in the vial, check the syringe for air bubbles. Gently tap the syringe to make any bubbles rise to the top of the syringe, near the needle. Slowly press the plunger to push the bubbles out of the syringe and into the vial. When you do this, if you accidentally push some solution back into the vial, pull slowly back on the plunger to draw the solution back into the syringe.

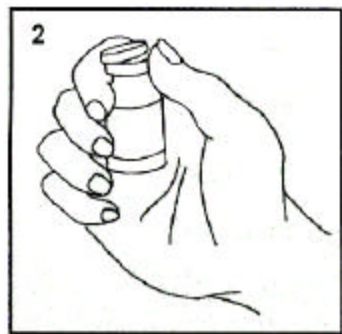


11. Pull the needle completely out of the vial. Again, **DO NOT** touch the needle or allow it to touch any surface.

**SKIP TO STEP 4 FOR INSTRUCTIONS ON HOW TO INJECT THE ENBREL DOSE.**

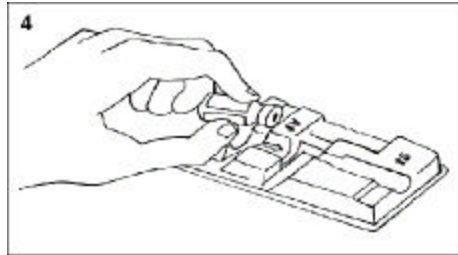
**Step 3B: Dose Preparation Guide (underside of the dose tray)**

1. Remove the contents of the tray and turn the tray over. The underside of the tray is a “Dose Preparation Guide.” It is specially designed to hold the vial and syringe in place while the ENBREL solution is prepared.
2. Remove the plastic cap from the ENBREL vial. Do not remove the gray stopper or metal ring around the top of the vial.

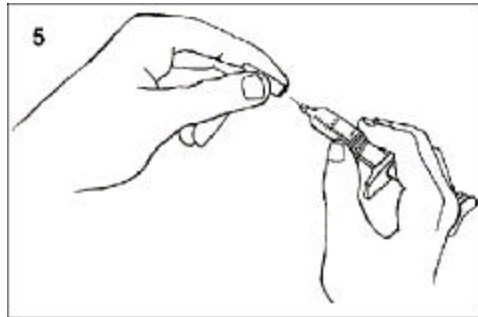


3. Use a new alcohol swab to clean the gray stopper on the ENBREL vial. After cleaning, do not touch the stopper with your hands.

4. Press the ENBREL vial into the space next to the ↓V mark in the Dose Preparation Guide; the gray stopper must face the center of the tray. Turn the vial so the stopper window is up and visible.



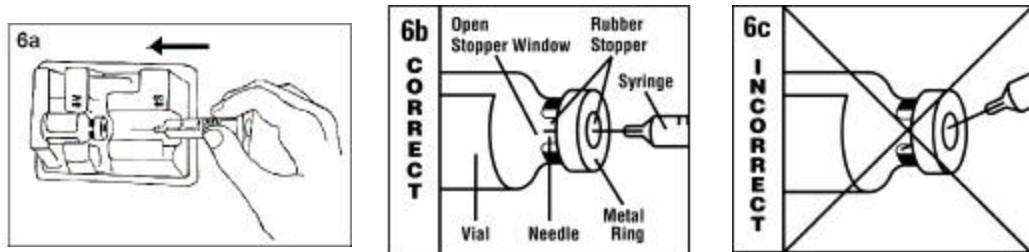
5. Pull the needle cover straight off the syringe. **DO NOT** touch the needle or allow it to touch any surface.



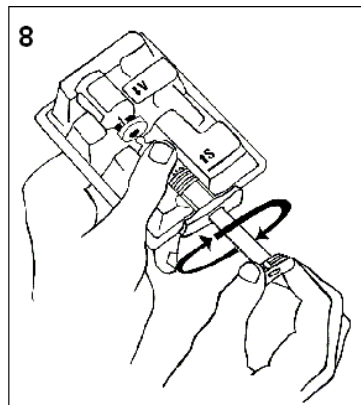
6. With the needle pointing at the gray stopper in the top of the vial, line up the “0.5 mL” mark on the syringe with the edge of the Dose Preparation Guide. Keep the syringe and needle level, so the needle does not touch the tray. Slide the syringe into the Dose Preparation Guide until the needle touches the center ring of the vial’s gray stopper. It may be necessary to rotate the vial slightly to get the needle correctly lined-up with the center of the stopper. If the needle is correctly lined up, you should feel a slight resistance and then a “pop” as you push the needle through the center of the stopper. If necessary, turn the vial again so the stopper window is

up and visible. Look for the needle tip inside the stopper window (see Illustration 6b).

If the needle is not correctly lined up with the center of the stopper, you will feel constant resistance as it goes through the stopper and no “pop”. The needle may then enter at an angle and bend, break, or prevent addition of diluent into the vial (see Illustration 6c).

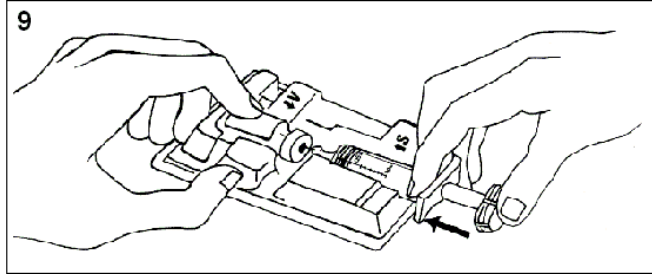


7. Slide the plunger into the syringe.
8. Turn the plunger clockwise until a slight resistance is felt. (That is, until more force is required to turn the plunger.)

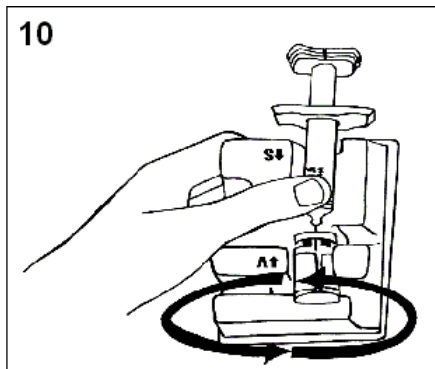


## ADDING DILUENT

9. Push the plunger down **VERY SLOWLY** until all the liquid from the syringe is in the vial. Adding the liquid too fast will cause a lot of foaming (bubbles).

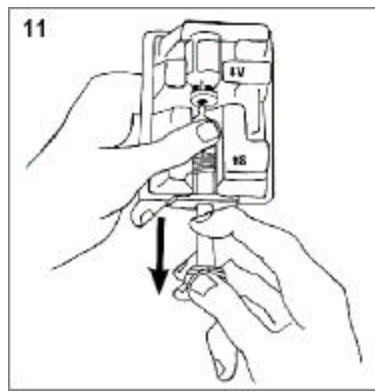


10. While holding the syringe in place, lift the Dose Preparation Guide so the vial is in an upright position. Gently move or swirl the Dose Preparation Guide in circles a few times, to dissolve the powder. **DO NOT SHAKE.** Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colorless. After the powder has completely dissolved, foam (bubbles) may still be present. This is normal. **Do not inject the solution if it contains lumps, flakes, or particles.** If all the powder in the vial is not dissolved or there are particles present, call 1-888-4ENBREL (1-888-436-2735) for assistance.



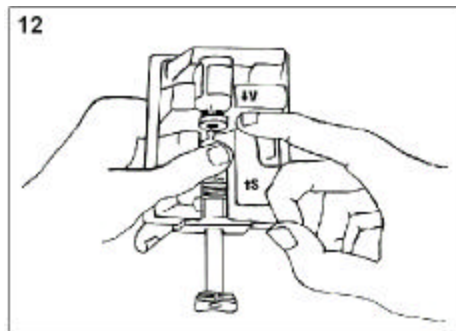
## WITHDRAWING THE ENBREL SOLUTION FROM THE VIAL

11. With the needle still in the vial, hold the Dose Preparation Guide with the vial upside down at eye level. Slowly pull the plunger back to draw the solution into the syringe. Use the “mL” markings on the side of the syringe to withdraw the appropriate dose as directed by your/your child’s doctor. For adult patients, remove the entire volume (1 mL of solution), unless otherwise directed by your doctor. For children, remove only the portion of the 1 mL solution as directed by your child’s doctor. Some white foam

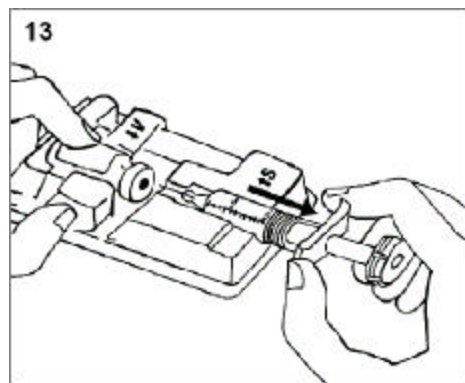


may remain in the vial—this is normal.

12. With the needle still inserted in the vial, check the syringe for air bubbles. Gently tap the syringe to make any bubbles rise to the top of the syringe, near the needle. Slowly press the plunger to push the bubbles out of the syringe and into the vial. When you do this, if you accidentally push some solution back into the vial, slowly pull back the plunger to draw the solution back into the syringe.

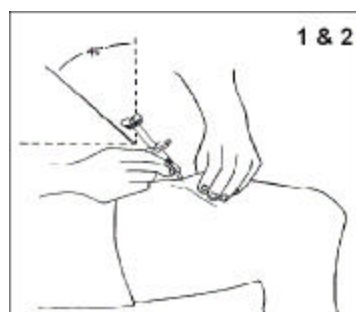


13. Slide the syringe out of the Dose Preparation Guide. Again, **DO NOT** touch the needle or allow it to touch any surface.

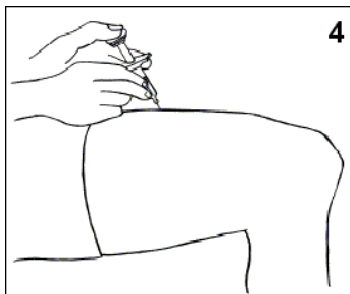


#### Step 4: Injecting the ENBREL Solution

1. With one hand, gently pinch the cleaned area of skin and hold it firmly. With the other hand, hold the syringe at about a 45° angle to the skin.
2. With a quick, short motion, push the needle into the skin.



3. Let go of the skin with the other hand.
4. With your free hand, slowly push the plunger down to inject the drug.



5. When the syringe is empty, remove the needle from the skin, being careful to keep it at the same angle it was when it was inserted.
6. Slight bleeding may occur. If needed, press a cotton ball over the injection site for 10 seconds. Do not rub the injection site. A bandage is optional.

### Step 5: Disposing of Supplies

1. The syringe and needle should **NEVER** be reused. **NEVER** recap a needle.
2. Immediately throw away the used syringe in a puncture-resistant container. A container made specifically for disposing of used syringes and needles may be used. **DO NOT** recycle the container.
3. Keep the container out of the reach of children. When the container is about two-thirds full, dispose of it as instructed by your/your child's doctor, nurse, or pharmacist. Follow any special state or local laws regarding the proper



disposal of needles and syringes.

4. ENBREL is supplied in a single-use vial that cannot be used more than once. After removing the dose needed, **any unused ENBREL should be discarded**. The ENBREL vials and used swabs should be placed in the trash, unless otherwise instructed by your/your child's doctor, nurse, or pharmacist. The dose tray and cover may be recycled.

All questions should be handled by a doctor, nurse, or pharmacist familiar with ENBREL. A toll-free information service is also available: 1-888-4ENBREL (1-888-436-2735).

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